Notice of Allowability	Application No. 10/010,942	Applicant(s) BASI ET AL.	
	Examiner Kimberly A. Ballard	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Applicant's response filed 3 March 2006*.

2. ☒ The allowed claim(s) is/are *13-41,62,169,171,173,175,177,179,181,183,185,187,189,191,193,195 and 197-215*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 12/22/05,3/3/06, 3/15/06.
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *5/4/06* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

EXAMINER'S AMENDMENT

Inventorship

In view of the papers filed 3 April 2006, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the deletion of Ted Yednock as a co-inventor.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Information Disclosure Statement

Signed and initialed copies of the IDS papers submitted 22 December 2005, 3 March 2006, and 15 March 2006 are enclosed in this action.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Debra Milasincic and Amy Mandragouras on 4 May 2006.

In the Specification:

On page 138, line 3, delete "ABSTRACT OF THE DISCLOSURE" and replace with --ABSTRACT--.

In the Claims:

Claims 6 and 7 have been cancelled without prejudice.

Claims 208-215 have been added.

The remaining claims, with the addition of claims 208-215, have been amended as follows:

13. A humanized immunoglobulin which specifically binds beta amyloid peptide (Aβ), or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding fragment comprising a light chain comprising

(i) the variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and

(ii) a variable framework region from a human acceptor immunoglobulin light chain, provided that at least three framework residues selected from the group consisting of L1, L2, L36 and L46 (Kabat numbering convention) are substituted with the corresponding amino acid residues from the mouse 3D6 light chain variable region sequence.

14. A humanized immunoglobulin which specifically binds amyloid beta peptide (Aβ), or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding fragment comprising a heavy chain comprising

(i) the variable region complementarity determining regions (CDRs) from the 3D6 heavy chain variable region sequence set forth as SEQ ID NO:4, and

(ii) a variable framework ~~regions~~ region from a human acceptor immunoglobulin heavy chain, provided that at least the framework residues H49, H93 and H94 (Kabat numbering convention) are substituted with the corresponding amino acid residues from the mouse 3D6 heavy chain variable region sequence.

15. The humanized immunoglobulin or antigen binding fragment of claim ~~6~~ 30, wherein the human acceptor light chain is of the subtype kappa II (Kabat convention).

16. The humanized immunoglobulin or antigen binding fragment of claim ~~7~~ 31, wherein the human acceptor heavy chain is of the subtype III (Kabat convention).

17. The humanized immunoglobulin or antigen binding fragment of claim 15, wherein the human acceptor light chain is selected from the group consisting of Kabat ID 019230, Kabat ID 005131, Kabat ID 005058, Kabat ID 005057, Kabat ID 005059, Kabat ID U21040 and Kabat ID U41645.

18. The humanized immunoglobulin or antigen binding fragment of claim ~~15~~ 17, wherein the human acceptor light chain is Kabat ID 019230.

19. The humanized immunoglobulin or antigen binding fragment of claim 16, wherein the human acceptor heavy chain is selected from the group consisting of Kabat ID 045919, Kabat ID 000459, Kabat ID 000553, Kabat ID 000386 and Kabat ID M23691.

20. The humanized immunoglobulin or antigen binding fragment of claim ~~16~~ 19, wherein the human acceptor heavy chain is Kabat ID 045919.

21. The humanized immunoglobulin or antigen binding fragment of claim ~~6~~ 30, wherein the light chain variable region comprises at least one rare human framework residue ~~in the light chain~~ and wherein the rare human framework residue is substituted with an amino acid residue which is common for human variable light chain sequences at that position.

22. The humanized immunoglobulin or antigen binding fragment of claim ~~6~~ 30, wherein the light chain variable region comprises at least one rare human framework residue ~~in the light chain~~ and wherein the rare human framework residue is substituted with a corresponding amino acid residue from a germline variable light chain sequence.

23. The humanized immunoglobulin or antigen binding fragment of claim 22, wherein the germline variable light chain sequence is selected from the group consisting of A1, A17, A18, A2, and A19.

24. The humanized immunoglobulin or antigen binding fragment of claim ~~7~~ 31, wherein the heavy chain variable region comprises at least one rare human framework residue ~~in the heavy chain~~ and wherein the rare human framework residue is substituted with an amino acid residue which is common for human variable heavy chain sequences at that position.

25. The humanized immunoglobulin or antigen binding fragment of claim ~~7~~ 31, wherein the heavy chain variable region comprises at least one rare human framework residue ~~in the heavy chain~~ and wherein the rare human framework residue is substituted with a corresponding amino acid residue from a germline variable heavy chain sequence.

26. The humanized immunoglobulin or antigen binding fragment of claim 25, wherein the germline variable heavy chain sequence is selected from the group consisting of VH3-48, VH3-23, VH3-7, VH3-21 and VH3-11.

27. The humanized immunoglobulin or antigen binding fragment of claim ~~25~~ 26, wherein the germline variable heavy chain sequence is VH3-23.

28. The humanized immunoglobulin or antigen binding fragment of claim 21, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human light chain variable region sequences in the light chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the light chain variable region subgroup.

29. The humanized immunoglobulin or antigen binding fragment of claim 24, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human heavy chain variable region sequences in the heavy chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the heavy chain variable region subgroup.

30. A humanized immunoglobulin which specifically binds beta amyloid peptide (Aβ), or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding fragment comprising a light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L1, L2, L36 and L46 (Kabat numbering convention) from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin.

31. A humanized immunoglobulin which specifically binds beta amyloid peptide (Aβ), or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding

fragment comprising a heavy chain comprising the complementarity determining regions (CDRs) and variable region framework residues H49, H93 and H94 (Kabat numbering convention) from the monoclonal antibody 3D6 heavy chain, wherein the remainder of the heavy chain is from a human immunoglobulin.

32. A humanized immunoglobulin which specifically binds beta amyloid peptide, or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding fragment comprising a light chain selected from the group consisting of:

(a) a light chain comprising the variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and a variable framework ~~regions~~ region from a human acceptor immunoglobulin light chain, provided that at least three framework residues selected from the group consisting of L1, L2, L36 and L46 (Kabat numbering convention) are substituted with the corresponding amino acid residues from the mouse 3D6 light chain variable region sequence; ~~and~~

(b) a light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L1, L2, L36 and L46 (Kabat numbering convention) from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin; and

(c) a light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L2, L36 and L46 (Kabat numbering convention)

from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin,

and a heavy chain selected from the group consisting of:

(a) a heavy chain comprising the variable region complementarity determining regions (CDRs) from the 3D6 heavy chain variable region sequence set forth as SEQ ID NO:4, and a variable framework ~~regions~~ region from a human acceptor immunoglobulin heavy chain, provided that at least the framework residues H49, H93 and H94 (Kabat numbering convention) are substituted with the corresponding amino acid residues from the mouse 3D6 heavy chain variable region sequence; and

(b) a heavy chain comprising the complementarity determining regions (CDRs) and variable framework residues H49, H93 and H94 (Kabat numbering convention) from the monoclonal antibody 3D6 heavy chain, wherein the remainder of the heavy chain is from a human immunoglobulin.

33. The humanized immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}.

34. The humanized immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^8 M^{-1}.

35. The humanized immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^9 M^{-1}.

36. The humanized immunoglobulin or antigen binding fragment of claim 32, wherein the heavy chain isotype is $\gamma 1$.

37. The humanized immunoglobulin or antigen binding fragment of claim 32, which binds to both soluble beta amyloid peptide (Aβ) and aggregated Aβ.

38. The humanized immunoglobulin or ~~an~~ antigen binding fragment of claim 37, wherein the soluble beta amyloid peptide (Aβ) is disaggregated Aβ.

39. The humanized immunoglobulin or antigen binding fragment of claim 32, which mediates phagocytosis of beta amyloid peptide (Aβ).

40. The humanized immunoglobulin or antigen binding fragment of claim 32, which crosses the blood-brain barrier in a subject.

41. The humanized immunoglobulin or antigen binding fragment of claim 32, which reduces both beta amyloid peptide (Aβ) burden and neuritic dystrophy in a subject.

62. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim 32 and a pharmaceutical carrier.

169. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 13, wherein the human acceptor light chain is of the subtype kappa II (Kabat convention).

171. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 14, wherein the human acceptor heavy chain is of the subtype III (Kabat convention).

173. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 169, wherein the human acceptor light chain is selected from the group consisting of Kabat ID 019230, Kabat ID 005131, Kabat ID 005058, Kabat ID 005057, Kabat ID 005059, Kabat ID U21040 and Kabat ID U41645.

175. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim ~~169~~ 173, wherein the human acceptor light chain is Kabat ID 019230.

177. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 171, wherein the human acceptor heavy chain is selected from the group consisting of Kabat ID 045919, Kabat ID 000459, Kabat ID 000553, Kabat ID 000386 and Kabat ID M23691.

179. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim ~~171~~ 177, wherein the human acceptor heavy chain is Kabat ID 045919.

181. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 13, wherein the light chain variable region comprises at least one rare human framework residue ~~in the light chain~~ and wherein the rare human framework residue is substituted with an amino acid residue which is common for human variable light chain sequences at that position.

183. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 13, wherein the light chain variable region comprises at least one rare human framework residue ~~in the light chain~~ and wherein the rare human framework residue is substituted with a corresponding amino acid residue from a germline variable light chain sequence.

185. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 183, wherein the germline variable light chain sequence is selected from the group consisting of A1, A17, A18, A2, and A19.

187. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 14, wherein the heavy chain variable region comprises at least one rare human framework residue ~~in the heavy chain~~ and wherein the rare human framework residue is substituted with an amino acid residue which is common for human variable heavy chain sequences at that position.

189. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 14, wherein the heavy chain variable region comprises at least one rare human framework residue ~~in the heavy chain~~ and wherein the rare human framework residue is substituted with a corresponding amino acid residue from a germline variable heavy chain sequence.

191. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 189, wherein the germline variable heavy chain sequence is selected from the group consisting of VH3-48, VH3-23, VH3-7, VH3-21 and VH3-11.

193. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim ~~189~~ 191, wherein the germline variable heavy chain sequence is VH3-23.

195. The ~~light chain~~ humanized immunoglobulin or antigen binding fragment of claim 181, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human light chain variable region sequences in the light chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the light chain variable region subgroup.

197. The ~~heavy chain~~ humanized immunoglobulin or antigen binding fragment of claim 187, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human heavy chain variable region sequences in the heavy chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the heavy chain variable region subgroup.

198. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~33~~ 25 and a pharmaceutical carrier.

199. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~34~~ 13 and a pharmaceutical carrier.

200. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~35~~ 14 and a pharmaceutical carrier.

201. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim 36 and a pharmaceutical carrier.

202. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~37~~ 30 and a pharmaceutical carrier.

203. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~38~~ 31 and a pharmaceutical carrier.

204. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~39~~ 207 and a pharmaceutical carrier.

205. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~40~~ 21 and a pharmaceutical carrier.

206. A pharmaceutical composition comprising the humanized immunoglobulin or ~~an~~ antigen binding fragment of claim ~~41~~ 22 and a pharmaceutical carrier.

207. A humanized immunoglobulin which specifically binds to beta amyloid peptide (Aβ), or antigen binding fragment thereof, the humanized immunoglobulin or antigen binding fragment comprising a light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L2, L36 and L46 (Kabat numbering convention) from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin.

208. A pharmaceutical composition comprising the humanized immunoglobulin or antigen binding fragment of claim 24 and a pharmaceutical carrier.

209. The humanized immunoglobulin or antigen binding fragment of claim 207, wherein the human acceptor light chain is of the subtype kappa II (Kabat convention).

210. The humanized immunoglobulin or antigen binding fragment of claim 209, wherein the human acceptor light chain is selected from the group consisting of Kabat ID 019230, Kabat ID 005131, Kabat ID 005058, Kabat ID 005057, Kabat ID 005059, Kabat ID U21040 and Kabat ID U41645.

211. The humanized immunoglobulin or antigen binding fragment of claim 210, wherein the human acceptor light chain is Kabat ID 019230.

212. The humanized immunoglobulin or antigen binding fragment of claim 207, wherein the light chain variable region comprises at least one rare human framework residue and wherein the rare human framework residue is substituted with an amino acid residue which is common for human variable light chain sequences at that position.

213. The humanized immunoglobulin or antigen binding fragment of claim 207, wherein the light chain variable region comprises at least one rare human framework residue and wherein the rare human framework residue is substituted with a corresponding amino acid residue from a germline variable light chain sequence.

214. The humanized immunoglobulin or antigen binding fragment of claim 213, wherein the germline variable light chain sequence is selected from the group consisting of A1, A17, A18, A2, and A19.

215. The humanized immunoglobulin or antigen binding fragment of claim 212, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human light chain variable region sequences in the light chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the light chain variable region subgroup.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kimberly Ballard, Ph.D.
Art Unit 1649
May 9, 2006